

May 17, 2005

Andy Wang, Ph.D.
Manager, Regulatory Affairs
Supresta
420 Saw Mill River Road,
Ardsley, NY 10502

Dear Dr. Wang:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Dimethyl methylphosphonate posted on the ChemRTK HPV Challenge Program Web site on March 8, 2004. I commend the DMMP Consortium for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the DMMP Consortium advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Mark Townsend, Acting Chief of the HPV Chemicals Branch, at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission: Dimethyl Methylphosphonate

Summary of EPA Comments

The sponsor, The DMMP Consortium, submitted a test plan and robust summaries to EPA for Dimethyl methylphosphonate (DMMP; CAS No. 756-79-6) dated January 26, 2004. EPA posted the submission on the ChemRTK HPV Challenge Web site on March 8, 2004.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. The submitter needs to provide measured data for the melting point and ready biodegradation endpoints.
2. Health Effects. Adequate data are available for acute, genetic and developmental toxicity for the purposes of the HPV Challenge Program. The submitted data are inadequate to address repeated-dose and reproductive toxicity. The submitter needs to provide adequate data for these endpoints. In addition, the submitter needs to address deficiencies in the robust summaries.
3. Ecological Effects. Adequate data are available for fish toxicity for the purposes of the HPV Challenge Program; however, the submitter needs to provide missing robust summary data elements. EPA agrees with the submitter's proposal to test for the aquatic invertebrate and green algae toxicity endpoints.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Dimethyl Methylphosphonate Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data submitted for boiling point, vapor pressure, partition coefficient, and water solubility are adequate for the purposes of the HPV Challenge Program.

Melting point. No data were submitted; the submitter needs to provide measured melting point data for this chemical. An estimated melting point value is acceptable if below 0 °C.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

EPA agrees with the submitter's proposal to provide modeled data for photodegradation and fugacity and recommends using a Level III model for fugacity. EPA also agrees with the submitter's approach to the stability in water endpoint (acquisition of peer-reviewed literature data).

Biodegradation. The activated sludge–respiration inhibition test (OECD TG 209) measures microbial toxicity, not biodegradation. The submitter needs to provide measured ready biodegradation data following OECD TG 301.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available to address acute, genetic, and developmental toxicity for the purposes of the HPV Challenge Program. The submitter needs to provide adequate data to address repeated-dose and reproductive toxicity. The submitter needs to address deficiencies in the robust summaries.

Repeated-dose toxicity. The submitted data for the 13-week repeated-dose toxicity study were compromised by SDA virus infection in the test animals, and the 2-year carcinogenicity bioassay (NTP) did not provide information on repeated-dose toxicity. Therefore, the submitter needs to provide data for this endpoint and EPA suggests a 90-day repeated-dose oral toxicity study following OECD TG 408, with specific attention to histopathological examination of male and female reproductive organs to address the reproductive toxicity endpoint (see below).

Reproductive toxicity. The submitted NTP studies evaluated only male animals, with positive results. No data are available for female reproductive toxicity. Information from the reproductive organs examination of both sexes from the 90-day repeated-dose toxicity study suggested above, with the existing adequate developmental toxicity data, would address this endpoint for the purposes of the HPV Challenge Program.

Ecological Effects (fish, invertebrates, and algae)

Adequate data are available for the fish toxicity endpoint for the purposes of the HPV Challenge Program. However, the robust summary needs to be enhanced. EPA agrees with the submitter's proposal to test for aquatic invertebrate and green algae toxicity. The proposed tests should be conducted in accordance with OECD TG's 202 and 201, respectively.

Specific Comments on the Robust Summaries

Physicochemical Properties

Partition coefficient. Page 3, Dimethyl methylphosphate should be Dimethyl methylphosphonate.

Health Effects

Acute toxicity. Missing information includes the purity of the test material, signs of toxicity, and whether body weights were taken and the necropsy was performed and the results.

Genetic toxicity. One or more robust summaries for *in vitro* studies lack the following information: the purity of the test material, the strains tested, the actual concentrations tested, the cytotoxic concentration, the number of replicates/concentration, the number of colonies counted or number of cells examined, the names of the positive controls and their responses, and the criteria for evaluating results.

Summaries for the *in vivo* sex-linked recessive lethal test and the cytogenicity assay (chromosomal aberration) lacked the following information: purity of the test material, detailed description of the experimental design, concentrations tested, information on positive and negative controls with their responses, time of exposure, number of cells examined, and criteria for evaluating results.

Reproductive toxicity. Robust summaries for the NTP studies did not identify the purity of the test material, or clearly describe the experimental design (especially the timing of exposure with respect to mating and termination).

Developmental toxicity. The summary for a developmental study in rats omitted the test material purity.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.